NASAL DELIVERY OF XYLITOL

The present invention claims priority to U.S. provisional application No. 60/106,388, filed Oct. 30, 1998.

FIELD OF THE INVENTION

The present invention relates generally to the art of intranasal delivery of bio-effecting agents to a mammal and, in particular, to an intranasal treatment and composition which rely on the effects of sugar alcohols, especially xylitol.

BACKGROUND OF THE INVENTION

Sugar alcohols, also known as polyols, are utilized in a variety of fields. The use of these polyhydric alcohols, such as sorbitol, mannitol, and xylitol, as non-fermentable carbohydrates in place of sucrose and other sugars in chewing gums and confections is known. For the most part sugar alcohols have been known and used based on their unique, substantially non-nutritional sweetening properties.

For example, xylitol, which is a five carbon chain classified as a polyol or sugar alcohol (commonly known as birch sugar because it can be derived from birch), is used as a sweetener because it possesses a sweetness equivalent to that of sucrose. Due to its five-carbon sugar alcohol structure, xylitol is unsuitable as a source of energy for most oral microorganisms. Regular consumption of xylitol has also been shown to reduce the incidence of dental caries. This is primarily attributed to xylitol's ability to inhibit and/or reduce the growth and acid production of *S. mutans*, which is the most important bacterium taking part in the pathomechanism of dental caries.

Xylitol similarly inhibits the growth of *Streptococcus pneumonia* in vitro during its logarithmic growth phase. The *S. pneumonia* bacteria species is believed to be the causative agent of certain types of pneumonia and upper respiratory infections, and is associated with other infectious diseases such as meningitis and sepsis. Furthermore it is believed to account for about 30% of all acute otitis media (AOM) episodes. Nasopharyngeal carriage of pneumococci has been shown to be a predisposing factor for AOM in children in a day care center.

Otitis media involves inflammation of the middle ear portion of the ear. The middle ear, or tympanum, is an irregular cavity which is filled with air, and communicates with the nasopharynx by the eustachian tube. Functionally speaking, the tympanum is traversed by a chain of movable bones, which connect the membrana tympani with the labyrinth, or inner ear, and serve to convey the vibrations communicated to the membrana tympani across the cavity of the tympanum to the internal ear.

Upper respiratory infections including otitis media are very prevalent in children. As mentioned above, many cases are believed to be caused by the *S. Pneumonia* bacteria. U.S. Pat. No. 5,719,196, issued to Uhari et al., has established that by using oral dosages of an effective amount of xylitol, respiratory infections such as otitis media may be effectively treated. The patent discloses that xylitol exhibits a growth inhibiting effect against pneumococci which reduces the pneumococcal carriage rates and also reduces the incidence of infection. The Uhari patent claims oral administration in the form of a solid, liquid, or as a chewing gum.

The nose is a reservoir for infectious agents. It is a source of entry for viral and microbial dissemination to the upper and lower respiratory tracts. The nasal carriage rate in infants can be as high as 70–90%, and declines with age. At three years of age, up to 40% of children carry pneumococci in their nasopharynx. This may explain the higher rate of acute otitis media and respiratory infections in younger children. The major respiratory pathogens, *S. pneumonia, H. influenza* and *S. pyogenes* are commonly found in the nasopharynx of children (45–90%, 15–70% and 3–50%, respectively) and also to a lesser extent in adults (15–25%, 6–40% and 6%, respectively).

It is, therefore, an intention of the present invention to provide improved composition(s) and method for treating respiratory infections including otitis media in mammals (e.g., humans) by nasally administering xylitol.

SUMMARY OF THE INVENTION

The present invention is a method and a composition for preventing and/or treating respiratory infections and otitis media in a mammal, especially human, by nasal administration of xylitol. In order to effectively administer xylitol nasally, it is formulated with one or more pharmaceutically acceptable carriers suitable for intranasal delivery.

Preferably the carrier includes a buffer (to maintain the pH of the composition), a thickening agent, a bioadhesive and a humectant. A pharmaceutically acceptable surfactant and a preservative may also be included along with one or more excipients suitable for a pharmaceutical composition.

Preferable buffers for maintaining the pH of the composition may be selected from the group consisting of acetate, citrate and phosphate buffers.

Preferably, thickening agents may be included and selected from the group consisting of methylcellulose, xantham gum, carboxy methylcellulose, polyvinyl alcohol, hydroxypropyl cellulose, carbomer, starches, chitosans, acrylates, and mixtures thereof. These excipients may also function as bioadhesives.

A suitable humectant can be selected from the group consisting of sorbitol, propylene glycol, glycerol, and mixtures thereof. Additionally, the surfactant can be anionic, cationic, or nonionic and is preferably selected from the group consisting of polyoxyethylene derivatives and fatty acid, partial esters of sorbitol anhydrides. For example, the surfactant can be selected from the group consisting of sodium lauryl sulfate, Tween 80, polyoxyl Stearate, polyoxy ethylene 50, fusieates, bila salts, and Octoxynol.

Preferably, the dosage rate administered to the host can be in an amount of from about 1 mg to about 10 g, more preferably from about 1 mg to about 2 g, and most preferably from about 1 mg to about 1 g. Such dosages can be administered in nasal compositions having a concentration of xylitol of from about 0.001% to about 10% by weight, more preferably from about 0.001% to about 2% by weight, and most preferably from about 0.001% to about 1% by weight.

The regimen of choice includes application of a nasal spray or gel at a frequency rate from once daily to about 4 times per day.

As a result of the present invention, a highly effective and efficient method of treatment for respiratory infections and otitis media is provided by nasal administration of xylitol. The present invention permits the delivery of xylitol more proximal to the biological area requiring treatment than by oral administration.

For a better understanding of the present invention, together with other and further objects and advantages, reference is made to the following detailed description,